UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION II
290 BROADWAY
NEW YORK, NEW YORK 10007-1866

December 4, 2015

BY ELECTRONIC MAIL

Robert Law, Ph.D.
demaximis, inc.
186 Center Street, Suite 290
Clinton, New Jersey 08809

Re: Lower Passaic River Study Area (LPRSA) 17-Mile draft Baseline Human Health Risk Assessment (BHHRA) – Cooperating Parties Group (CPG) letter dated November 11, 2015 regarding EPA comments on the draft BHHRA

Dear Dr. Law:

The U.S. Environmental Protection Agency (EPA) is in receipt of the CPG's November 11, 2015 letter whereby a summary of the CPG's understanding of the previous agreements on the draft BHHRA comments/responses was provided as were specific comments/responses where further action is needed.

The summary and comment/responses contained in the November 11, 2015 letter have been reviewed and found to be generally acceptable, except for the following comments identified below. Outlined below are EPA's recommendations for addressing these comment/responses for inclusion in the revised draft BHHRA.

- **Comment/Response #42** – With respect to item 1 under Comment #42, EPA will review the modification incorporated into the revised draft BHHRA text, once received. Please note that EPA does not agree with the conclusions drawn by the CPG that consumption is not expected to be suppressed by the presence of the advisory. In particular, EPA disagrees with the CPG's interpretation of the conclusions from the Connelly et al. 1996 publication.

  With respect to item 3 under Comment #42, EPA maintains the position that the phrase "under current conditions" at the end of the "Crab Consumption Rate" should be included in the referenced text. This position was previously provided in an October 30, 2015 email from Stephanie Vaughn to Robert Law.

- **Comment/Response #87c** – Please see Enclosure 1, which includes clarification that the chlordane relative potency factors shall apply only to the noncancer assessment. Enclosure 1 also includes clarification that the largest relative potency factor (RPF) value among male and female shall be used. RPFs to be used are: 4.8 for *cis*-nonachlor, 32.2 for *trans*-nonachlor and 5.6 for oxychlordane.

- **Comment/Response #151** – Please see Enclosure 2 for EPA's edits to the CPG's language for inclusion in the draft BHHRA to address this comment/response. As noted in your letter dated November 11, 2015, EPA did provide the revised language to National Center for Environmental Assessment (NCEA) for review, and our edits are based on the feedback received from NCEA.

  EPA's recommendation to modify the text for arsenic is based on the consideration that the language does not address the carcinogenicity related to lung and bladder cancers. Additionally, the CPG's text was based on a single paper published in 2008. EPA selected the Science Advisory Board's (SAB) evaluation that reflects an up-to-date evaluation of the available information including Mode of Action (page 9). Also, the term "nonlinear" should be used in place of threshold. (Note that sentence previously suggested by EPA about the review of inorganic arsenic, which the CPG included in its proposed language responding to Comment #151, is now addressed with alternate language in EPA's edits for Comment #151.)

  EPA's recommendation to modify the text for dioxin is based on the consideration that the SAB recommendations were developed after the quoted publications.

- **Comment/Response #154** – Please see Enclosure 3 for EPA's edits to the CPG's language for inclusion in the draft BHHRA regarding a cancer slope factor for dioxin based on EPA's discussion with the Office of Superfund Remediation and Technology Innovation (OSRTI).

Please incorporate EPA's recommendations provided herein into the revised draft BHHRA. The EPA looks forward to receiving the revised draft BHHRA for review on December 18, 2015.

Please let me know if you have any questions.

Sincerely,

Jennifer LaPoma

Jennifer LaPoma, Remedial Project Manager
Lower Passaic River Study Area RI/FS

Enclosure

Enclosure 1

Superfund Technical Support Center

National Center for Environmental Assessment
U.S. Environmental Protection Agency
26 West Martin Luther King Drive, MS-AG41
Cincinnati, Ohio 45268

Phillip Kaiser/Hotline Director, Teresa Shannon/Administrator
Hotline 513-569-7300, FAX 513-569-7159, E-Mail: Superfund_STSC@epa.gov

November 24, 2015

Marian Olsen
Region 2

ASSISTANCE REQUESTED: Inquiry as to whether the cancer risks of chlordane should be evaluated and if relative potency factors can be applied on the finding of hypertrophy for nonachlor.

ENCLOSED INFORMATION: Attachment 1: OlsenMarian_CancerRPFsResponseFinal.pdf

If you have any questions regarding this transmission, please contact the STSC at (513) 569-7300.

Attachments (1)

cc: STSC files

Supported by Highlight Technologies, LLC, under
U.S. Environmental Protection Agency Contract No. EP-C-13-007

Question:
Since the study (to derive RPFs) was based on a subchronic 28 day study should we evaluate the cancer risks? Chlordane, has both a cancer slope factor and oral Reference Dose. Can we apply the RPFs for cancer based on the finding of hypertrophy for nonachlor?

Response:
The RPFs (relative potency factors) were derived based on a 28-day study using incidence of hepatocellular hypertrophy in rats. It is unclear if these RPFs that were derived for a noncancer endpoint (i.e., hepatocellular hypertrophy) would be applicable to a cancer risk value due to the lack of cancer data for the chemicals in question (e.g., oxychlordane). Due to this uncertainty, the STSC cannot recommend that these RPFs be used to derive surrogate cancer risk values.

Superfund Technical Support Center

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November 12, 2015

Marian Olsen
Region 2

ASSISTANCE REQUESTED: Clarification on the use of male or female relative potency factors to derive surrogate points of departure.

ENCLOSED INFORMATION: Attachment 1: OlsenMarian_RPFsResponseFinal.pdf

If you have any questions regarding this transmission, please contact the STSC at (513) 569-7300.

Attachments (1)

cc:

Supported by Highlight Technologies, LLC, under
U.S. Environmental Protection Agency Contract No. EP-C-13-007

Question:
Whether to use male or female specific relative potency factor (RPFs) to derive surrogate points of departure (PODs) for *cis*-nonachlor, *trans*-nonachlor, and oxychlordane compounds.

Response:
Based on the RPFs derived by the STSC in the previous analysis, it was determined that gender differences in toxicity potencies exist for rats treated with *cis*-nonachlor or *trans*-nonachlor. The application of the largest RPF among male and female rats will result in a lower surrogate POD for both sexes. Therefore to be health protective, it is recommended to use the largest RPF value among male and female rats to identify surrogate PODs; specifically 4.8 for *cis*-nonachlor and 32.2 for *trans*-nonachlor. Because data were only available in female rats to derive a RPF for oxychlordane, it is recommended to use the RPF of 5.6 for female rats to determine surrogate PODs for this chemical.

Enclosure 2

Comment #151 – Proposed revised text for first and second full paragraphs on p. 7-34 (third and fourth paragraphs of Section 7.3.2.3)

USEPA's current carcinogen risk assessment guidelines (USEPA 2005b) emphasizes mode of action data, and recognizes that some carcinogens may act in a nonlinear fashion. Therefore, it is recognized that some carcinogens may have a nonlinear ~~threshold~~ dose below which effects would not be seen. For example, a nonlinear dose ~~threshold~~ for carcinogenic activity has been demonstrated for chloroform and was used as the basis for USEPA's development of dose-response values for chloroform (USEPA 201~~3~~5a).

EPA's IRIS program includes multiple steps including a systematic literature review in the development of individual Chemical Files (USEPA 2015a). For example, EPA is updating the chemical assessment for inorganic arsenic based on the 2011 Science Advisory Board recommendations (SAB letter to Administrator Lisa Jackson Regarding the Review Comments on EPA's Responsiveness to SAB 2007 Recommendations for the Revision of Cancer Assessment of Inorganic Arsenic (available at: http://yosemite.epa.gov/sab/sabproduct.nsf/fedrgstr_activites/9FCEE4E20ABD6EB48525784600791AC2/$File/EPA-SAB-11-003-unsigned.pdf). In addition, dioxin is listed on the IRIS agenda and the evaluation will consider the recommendations from the August 2011 SAB letter to EPA's Administrator Lisa Jackson regarding the SAB's Review of EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments (May 2010) available at: http://yosemite.epa.gov/sab/SABPRODUCT.NSF/2A45B492EBAA8553852578F9003ECBC5/$File/EPA-SAB-11-014-unsigned.pdf .

~~There is significant epidemiological evidence that a threshold exists for the potentially carcinogenic effects of arsenic (Boyce et al. 2008). Although USEPA does not currently recognize the potential for a threshold for the carcinogenic effects of arsenic, it is mentioned here as a potential source of uncertainty in the risk assessment. USEPA is currently reviewing the toxicity of inorganic arsenic through the IRIS process (USEPA 2015a).~~

~~The potential for a nonlinear mode of action has also been raised for TCDD (NRC 2006; WHO Joint Expert Committee on Food Additives (JECFA) 2001; European Commission Health & Consumer Protection Directorate (EC-SCF) 2001; Simon et al. 2009; Popp et al. 2006; Pohl et al. 2002). Based on models that assume a threshold for effects, including cancer, a range of tolerable daily intakes for TCDD have been developed (JECFA 2001; EC-SCF 2001; Simon 2009). The toxicity of TCDD remains a complex topic, with many research publications on the nature of the adverse effects caused by exposure, the mechanism of action, and the dose-response relationships. The cancer assessment for dioxin is currently being re-evaluated by USEPA (USEPA 2015a). There is also support in the scientific literature for a threshold mechanism of action for TCDD. Simon, et al. (2009) derived a non-linear RfD of 100 pg/kg-day (1E-07 mg/kg-day) for TCDD using a benchmark dose approach and NTP (2006a, b, c) rat cancer bioassay data. Benchmark dose values were developed for key events in the tumor promotion~~

~~mode of action of TCDD. This RfD is consistent with the 2006 National Research Council and the 2011 SAB panel's recommendation to develop a threshold-based cancer potency factor for TCDD and with the methodology in USEPA's Cancer Guidelines (USEPA 2005b). Other scientists support a threshold model for dioxin cancer effects (Pohl et al. 2002, Starr 2001, Popp et al. 2006). A report of the Joint Expert Committee on Food Additives (JECFA) of the WHO noted that "a tolerable intake could be established for TCDD on the basis of the assumption that there is a threshold for all effects, including cancer" (JECFA 2001). Similarly, the European Commission Health & Consumer Protection Directorate-General Scientific Committee on Food uses a threshold model for cancer risk (EC-SCF 2001). Thus, there is uncertainty in the use of CSFs for TCDD, arsenic, as well as other potentially carcinogenic COPCs, that were derived using linear extrapolation methods.~~

Enclosure 3

Draft BHHRA Comment 154 – EPA Suggested Replacement Text

7.3.6.1 Tier 3 Cancer Slope Factor for TCDD-TEQ

Dioxins and furans occur in the environment in complex mixtures. Although the members of this family of chlorinated compounds are considered to have a common mechanism of action, they differ in potency. By far, the most toxic and the most extensively studied of the group is 2,3,7,8-TCDD (TCDD). The toxicity of this congener is used as a reference point for evaluating the other compounds (USEPA 2010). TCDD was a major contributor to the cancer risks and non-cancer health hazards at the site from ingestion of fish and crabs.

In the absence of a Tier 1 or Tier 2 toxicity value, a Tier 3 value was selected by USEPA Region 2 as described below. [For an update on the status of USEPA's ~~ongoing~~ reassessment of dioxin CSF please refer to the IRIS Agenda at: www2.epa.gov/iris.] Consistent with USEPA's toxicity values hierarchy guidance (2003a), a Tier 3 CSF was selected to calculate cancer risks from exposure to dioxin TEQ. Several potential Tier 3 CSFs for 2,3,7,8-TCDD are listed in the response to #44 of the Frequently Asked Questions for USEPA's Regional Screening Levels (RSL) table (USEPA 2015b). Of the five listed values, two are not considered further. ~~here for the following reasons: (1) T~~the Minnesota CSF (MDH 2009) was based on a USEPA reassessment that has not been finalized. ~~; and (2) the~~ The Michigan CSF (MIDEQ 1998), ~~which was based on a re-analysis of the female rat liver tumors from Kociba et al. (1978) using an updated tumor classification scheme (Maronpot et al. 1986, EPA 1990),~~ has limited publicly available information.

~~A brief description of T~~the three other listed Tier 3 cancer slope factors, identified by USEPA on the RSL website's Frequently Asked Questions-, which were considered, are: ~~is provided below~~.

- *USEPA (1985)*
  USEPA's Office of Health and Environmental Assessment (currently the National Center for Environmental Assessment) developed an oral CSF for 2,3,7,8-TCDD of 156,000 $(mg/kg\text{-}day)^{-1}$ (USEPA 1985). ~~The CSF was based on the combined incidence of lung, palate, and nasal carcinomas, and liver hyperplastic nodules or carcinomas in female rats in the study by Kociba et al. (1978).~~

- *USEPA (1997b)*
  USEPA's Health Effects Assessment Summary Table, or HEAST, provides an oral CSF of 150,000 (mg/kg-day)-1 (USEPA 1997b). HEAST cites the 1985 USEPA Health Assessment Document described above.

- *California Environmental Protection Agency (2002)*

California Environmental Protection Agency (CalEPA), Office of Environmental Health and Hazard Assessment provides an oral CSF of 130,000 $(mg/kg\text{-}day)^{-1}$ for TCDD (CalEPA 2002). The CSF was based on the occurrence of hepatocellular adenomas and carcinomas in male mice in a study by the National Toxicology Program (NTP 1982).

The above three dioxin CSFs range from 130,000 to 156,000 $(mg/kg\text{-}day)^{-1}$. The differences in these CSFs will not significantly change the results of the risk assessment. For example, exposure to TCDD-TEQ via consumption of a mixed fish diet would results in the following cancer risks for the RME adult/child receptor. (Comment: Please update with appropriate exposure and risk values for receptor and diet) fish consumption, assuming a diet of 100% common carp, would result in the following calculated cancer risks for the RME adult angler:

Contaminant ~~Fish Tissue – Common Carp~~	Exposure (mg/kg-day)	Cancer Slope Factor $(mg/kg\text{-}day)^{-1}$	TCDD-TEQ Risk
TCDD-TEQ	1.91 x 10-8	130,000	2.48 x 10-3
TCDD-TEQ	1.91 x 10-8	150,000	2.87 x 10-3
TCDD-TEQ	1.91 x 10-8	156,000	2.98 x 10-3

As shown in the above table, the change in the calculated risk as a result of using the three different CSFs does not change the overall conclusion that the NCP risk range would be exceeded for the LPRSA RME adult/child angler consuming fish ~~who eats carp~~. Based on the above sensitivity analysis, as well as its use in the PCB-TEQ example in USEPA's PCB Cancer Reassessment (USEPA 1996) ~~of dioxin-like PCBs utilizes~~, the HEAST CSF was selected as the Tier 3 dioxin CSF ~~selected~~ for this site.

~~TCDD RfD~~

~~Consistent with the OSWER Directive regarding the selection of toxicity values, a Tier 1 toxicity value for 2,3,7,8-TCDD was selected to calculate the non-cancer health hazards. The IRIS RfD for 2,3,7,8-TCDD is 7×10^{-10} mg/kg-day and this was used in the calculation of non-cancer hazards associated with dioxin TEQs.~~

~~Dioxin TEFs~~

~~The calculation of dioxin TEFs followed the U.S. Environmental Protection Agency (EPA) Office of Science Advisor's Risk Assessment Forum's document titled *Recommended Toxicity Equivalence Factors (TEFs) for Human Health Risk Assessments of 2,3,7,8-Tetrachlorodibenzo-p-dioxin and Dioxin-Like Compounds* (EPA 2010). This document recommended the 2005 WHO consensus TEFs.~~

~~Arsenic~~

~~The assessment relied on the toxicity values in the Integrated Risk Information System (IRIS), a Tier 1 toxicity value identified in the OSWER directive, as the basis for evaluating the cancer risks and non-cancer health hazards from exposure to IRIS. Currently, EPA is re-evaluating the toxicity of arsenic through the IRIS process and it is premature to prejudge any potential changes to this toxicity value.~~